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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/505,446	09/01/2004	Antonio Ferrante	P26675CMH:KG	3217
7590	09/28/2006			
O M Sam Zaghmout BioIps 8509 Kernon Court Lorton, VA 22079			EXAMINER MARTIN, PAUL C	
			ART UNIT	PAPER NUMBER
			1655	

DATE MAILED: 09/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/505,446	<b>Applicant(s)</b> FERRANTE, ANTONIO	
	<b>Examiner</b> Paul C. Martin	<b>Art Unit</b> 1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 11 July 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 32-41 and 54-71 is/are pending in the application.
- 4a) Of the above claim(s) 32-41 and 54-62 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 63-71 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |                                                                                                            |                                                                                         |
|------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____                                                |

### **DETAILED ACTION**

Claims 32-41 and 54-71 are pending in this application, Claims 63-71 were examined on their merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All objections and rejections not repeated in the instant Action have been withdrawn due to the Applicant's response to the previous Action.

The Amendment filed 07/11/06 has been accepted and entered.

### **New Rejections necessitated by Applicant's Amendment**

This is a new rejection necessitated by the Applicant's amendment filed 07/11/06.

### ***Claim Rejections - 35 USC § 103***

Claims 63-68 and 71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Costabile *et al.* (2001) in view of Ghosh *et al.* (5,431,924).

Costabile *et al.* teaches an assay which measures the activity of an *in vitro* preparation of T-lymphocytes comprising the addition of *n*-3 polyunsaturated fatty acid  $\beta$ -oxa to the T-lymphocytes (Pg. 3981, Column 1, Lines 34-49), measurement of the change in the activity of the T-lymphocytes following addition of the  $\beta$ -oxa (Pg. 3983 Fig. 2A), and comparing the change in activity for the  $\beta$ -oxa treated cells against the change in activity for the known anti-inflammatory *n*-3 polyunsaturated fatty acid docosahexaenoic acid (DHA), the DHA having been measured in the same steps and used to generate a standard against which  $\beta$ -oxa effectiveness is measured (Pg. 3983, Fig. 2A) and the serial dilution of the fatty acids (Pg. 3983, Figs. 2a, 2b, 3a, 3b).

Costabile *et al.* teaches an assay wherein the substance is a biologically active component of oils (fatty acid) (Pg. 3981, Column 1, Lines 15-25) and dilution of the fatty acids in ethanol (Pg. 3981, Column 1, Lines 40-44).

Costabile *et al.* teaches an assay wherein the preparation is a preparation of T-lymphocytes and the activity is lympho-proliferation (Pg. 3981, Column 1, Lines 50-65).

Costabile *et al.* teaches an assay wherein the preparation is a preparation of T-lymphocytes and the activity is production of the cytokines IL-2, Interferon- $\gamma$ , and TNF- $\beta$  (Pg. 3981, Column 1, Lines 66-68 and Column 2, Lines 1-8).

Costabile *et al.* teaches wherein certain polyunsaturated fatty acids have been demonstrated to produce potent inhibitors of chemotaxis upon metabolization by neutrophils (Pg. 3986, Column 1, Lines 47-55) and that some polyunsaturated fatty acids are known to stimulate neutrophil activity while modified others lack that property (Pg. 3980, Column 2, Lines 8-27).

Costabile *et al.* does not teach wherein the substance is selected from animal or plant oils, selected from tea tree, linseed, borage, and evening primrose oils, fish oils, and algal, microbial and fungal oils, or wherein the substance is emu oil or an ethanol extract of emu oil.

Ghosh *et al.* teaches that eicopentaenoic acid (EPA) and docosahexanoic acid (DHA) are the principle long chain fatty acid triglycerides in fish oil and that dietary fish oil supplementation may support endogenous anti-inflammatory activity by modifying production of harmful mediators within the animal's tissues (Column 1, Lines 46-49 and 58-61). Further, Ghosh *et al.* teaches that an alternative pathway of unsaturated fatty acid metabolism is via the C18-triunsaturated fatty acids, gamma and alpha-linolenic acid, found in plant oils such as evening primrose oil (Column 2, Lines 3-6) and fish oils (Column 1, Lines 33-49) and tea tree and Linseed oils (Column 2, Lines 10-24) and in extracted emu oils (Column 2, Lines 41-44).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to adapt the assay for assessing the anti-inflammatory activity of a substance as taught by Costabile *et al.*, which measures the activity of an *in vitro* preparation of T-lymphocytes with the use of other polyunsaturated fatty acids from natural sources as taught by Ghosh *et al.* because the ordinary artisan would have been familiar with the use of isolated natural compounds from natural oils as the basis by which many new compounds can be refined from or synthesized in order to obtain more desirable experimental results. The ordinary artisan would have been motivated to use animal (emu) or plant oils in the method taught by Costabile *et al.* because of the benefit of obtaining a cheap, cost-effective source of polyunsaturated fatty acids. Indeed, Ghosh *et al.* discloses the control elements used by Costabile *et al.* as having known anti-inflammatory activities (Column 1, Lines 46-49). The ordinary artisan would have had a reasonable expectation of success based upon the similarity of the two methods in examining the effects of polyunsaturated fatty acids on t-lymphocyte cell preparations.

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

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Claims 63-69 and 71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Costabile *et al.* (2001) in view of Ghosh *et al.* (5,431,924) and Schmidt *et al.* (1989).

The teachings of Costabile *et al.* and Ghosh *et al.* were discussed above.

Neither Costabile *et al.* nor Ghosh *et al.* teach a method wherein the cells are neutrophils and the activity measured is chemotaxis.

Schmidt teaches a method for characterizing the anti-inflammatory activity of fish oil wherein polyunsaturated fatty acids are shown to inhibit neutrophil chemotaxis (Pg. 55, Column 1, Lines 1-8 and Table 1) and that macrophages and monocytes play an important role in atherosclerosis (Pg. 53, Column 1, Lines 1-3 and Column 2, Lines 13-15).

It would have been obvious to one of ordinary skill at the time the invention was made to combine the assay taught by Costabile *et al.* which measures the activity of an *in vitro* preparation of T-lymphocytes after exposure to polyunsaturated fatty acids, and Ghosh *et al.* who teaches that polyunsaturated fatty acids have known anti-inflammatory properties and can be found in plant and animal oils, with the method of characterizing the anti-inflammatory activity of fish oil on neutrophil chemotaxis taught by Schmidt *et al.* because the methods are drawn toward characterizing the anti-inflammatory activity of natural oil compounds on the various activities of certain types of cells from the immune system. The ordinary artisan would have been motivated to adapt the method of Costabile *et al.* to include the method of characterizing the anti-inflammatory activity of fish oil on neutrophil chemotaxis because of the advantage demonstrated by Schmidt *et al.* that polyunsaturated fatty acid compounds specifically inhibit neutrophil chemotaxis, a part of the inflammatory pathway and because Costabile *et al.* teaches that some metabolic byproducts of polyunsaturated fatty acids are known chemotaxis inhibitors. The ordinary artisan would have had a reasonable expectation of success based upon the similarities between the two methods and the success of the methods in determining anti-inflammatory activities separately.

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.



Claims 63-68, 70 and 71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Costabile *et al.* (2001) in view of Ghosh *et al.* (US 5,431,924) and Ferrante *et al.* (US 5,767,156).

The teachings of Costabile *et al.* and Ghosh *et al.* were discussed above.

Neither Costabile *et al.* nor Ghosh *et al.* teach a method wherein the cells are neutrophils and the activity measured is adherence to endothelial cells.

Ferrante *et al.* teaches wherein a polyunsaturated fatty acid is used to treat neutrophil preparations and stimulate neutrophil adherence to endothelial cells (Column 6, Lines 33-35 and Figs. 8&9).

It would have been obvious to one of ordinary skill at the time the invention was made to combine the assay taught by Costabile *et al.* which measures the activity of an *in vitro* preparation of T-lymphocytes after exposure to polyunsaturated fatty acids, and Ghosh *et al.* who teaches that polyunsaturated fatty acids have known anti-inflammatory properties and can be found in plant and animal oils, with the method of characterizing the effect of polyunsaturated fatty acids on neutrophil adherence to endothelial cells as taught by Ferrante *et al.* because all of the methods are drawn toward characterizing the anti-inflammatory activity of natural oil compounds on the various activities of certain types of cells from the immune system.

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The ordinary artisan would have been motivated to adapt the method of Costabile *et al.* to include the method of characterizing the anti-inflammatory activity of fish oil on neutrophil adherence to endothelial cells because of the advantage demonstrated by Ferrante *et al.* that certain polyunsaturated fatty acid compounds specifically stimulate neutrophil adherence to endothelial cells, a part of the inflammatory pathway and because Costabile *et al.* teaches that some polyunsaturated fatty acids have stimulatory effects on neutrophils, while certain modified polyunsaturated fatty acids lack this property. The ordinary artisan would have had a reasonable expectation of success based upon the similarities between the two methods and the success of the methods in determining anti-inflammatory activities separately.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

***Response to Arguments***

Applicant's arguments filed 07/11/06 have been fully considered but they are not deemed to be persuasive.

The Applicant argues that there is no suggestion to be found in the references that would suggest the use of the substances disclosed by Ghosh *et al.* in a standardized assay.

The Applicant's argument is not found to be persuasive because Costabile is directed toward the assay of the anti-inflammatory activity of polyunsaturated fatty acids, such as EPA and DHA and Ghosh *et al.* clearly discloses that eicopentaenoic acid (EPA) and docosahexanoic acid (DHA) are the principle long chain fatty acid triglycerides in fish oil and that dietary fish oil supplementation may support endogenous anti-inflammatory activity. As described above, the assay of Costabile essentially is an assessment of the anti-inflammatory properties of a substance (a new synthetic polyunsaturated fatty acid) as compared to a known polyunsaturated fatty acid using a series of diluted amounts.

The Applicant argues that there is no teaching or disclosure which would suggest the need or desirability of the control in the experimental process involving novel synthetic polyunsaturated fatty acids and that there appears to be no explicit direction to isolate polyunsaturated fatty acids from the substances described by Ghosh.

The Applicant's argument is not found to be persuasive because Costabile clearly teaches a control polyunsaturated fatty acid with known anti-inflammatory properties to which the new synthetic polyunsaturated fatty acid is compared to. Controls are well known in the scientific arts as a means of verifying if experimental data are due to the change of some condition. The fact that Ghosh does not explicitly teach the isolation of polyunsaturated fatty acids from the described substances is not relevant to the claims at hand, which do not limit the substances to only those which are isolated.

The Applicant argues that there is nothing to be found in the prior art references (Costabile and Schmidt, instantly) which establishes the need or desirability of using the methodology of Schmidt in the method of Costabile.

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The Applicant's argument is not found to be persuasive because Costabile teaches above that neutrophil metabolism of some polyunsaturated fatty acids results in the production of neutrophil chemotaxis inhibitors. Schmidt provides the specific experimental method by which this teaching is demonstrated using polyunsaturated fatty acids.

### ***Conclusion***

No Claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul C. Martin whose telephone number is 571-272-3348. The examiner can normally be reached on M-F 8am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Paul Martin  
Examiner  
Art Unit 1655

09/20/06



CHRISTOPHER R. TATE  
PRIMARY EXAMINER